REMARKS

Claims 1, 3-10, 13-14 are pending. Claims 2, 11, 12 and 25 are canceled in this amendment without prejudice to further prosecution in a related application(s). Claims 32 and 33 have been added through this amendment. Support for new Claims 32 and 33 can be found on page 21 of the specification as well as in the Examples. Claims 1, 3-9 and 14 have been amended to correct informalities and to provide clarification. Claims 1 and 14 have also been amended to identify a particular method used to remove embryonic trophectoderm. Support for this amendment can be found at page 6, lines 13-17, and elsewhere in the application. No new matter is disclosed by way of this amendment.

Specification

The Examiner objected to the specification for failure to comply with the sequence listing requirements under 37 CFR 1.821- 1.825. Applicant submits a Sequence Listing complying with 37 CFR 1.821- 1.825 in connection with this paper. This paper is accompanied by a floppy disk containing the above named sequence, SEQ ID NO: 1-3 in computer readable form, and a paper copy of the sequence information. The computer readable sequence listing was prepared through use of the software program "PatentIn" provided by the PTO. The information contained in the computer readable disk is identical to that of the paper copy. This amendment contains no new matter. Applicant submits that this amendment, the accompanying computer readable sequence listing, and the paper copy thereof serve to place this application in a condition of adherence to the rules 37 C.F.R. § 1.821-1.825. . Applicant requests that the Sequence Listing be entered into the Specification.

The Specification has been amended to introduce the SEQ ID NOs. to identify the sequences.

Claim Objection

The Examiner objected claim 2 as being of improper dependent form. Claim 2 has been cancelled, thus removing the objection.

35 U.S.C. § 112 - First paragraph

The Examiner rejected claims 1-14 under 35 U.S.C. § 112 - first paragraph, for lack of enablement. Specifically, the Examiner asserted that the specification, while being enabling for culturing the inner mass cells of a blastocyst embryo to establish embryonic stem cells, is not enabling for culturing any part of the blastocyst embryo. While not agreeing with propriety of the rejection, in the interest of expediting prosecution Applicant has amended claim 1 to recite "culturing at least a portion of said inner cell mass." Claim 14 has been similarly amended. Applicant asserts that the amendments address the Examiner's concerns and that claims are in compliance with 35 U.S.C. § 112 - first paragraph.

35 U.S.C. § 112 – Second paragraph

The Examiner rejected claims 1-14 under 35 U.S.C. § 112 - second paragraph, for failing to particularly point out and distinctly claim the subject matter the Applicant regards as his invention. Specifically, the Examiner asserted that claims are unclear because what the term "blastocyst embryo" encompasses in claim 1 is not clearly set forth in view of the limitations in claim 2. Applicant believes the Examiner's rejection has been obviated by the deletion of claim 2.

Applicant asserts that the claims are in compliance with 35 U.S.C. § 112 - second paragraph.

35 U.S.C. § 102

The Examiner has rejected Claim 25 as being anticipated by Thomson *et al.*

Claim 25 has been cancelled without prejudice to claim such subject matter in a separate application.

35 U.S.C. § 103

The Examiner rejected Claims 1~14 as lacking being obvious over Thomson *et al.* in view of Kaufmann *et al.* Applicant respectfully traverses.

To establish a *prima facie* case of obviousness under 35 U.S.C.§103, the Examiner must demonstrate a suggestion or motivation in the prior art to modify or combine the teachings of the references to arrive at the claimed invention. Further, the prior art must provide one of ordinary skill with a reasonable expectation of success. Applicant respectfully submits that the present invention is not obvious over the cited references, Thomson *et al.* and Kaufman *et al.*

The present invention sets forth (i) the use of a cryopreserved blastocyst embryo; (ii) the use of an anti-human lymphocyte antibody (AHLA) in removing trophectoderm from one embryo, thereby isolating inner cell mass; and (iii) the use of a STO cell (mouse embryonic fibroblast, # CRL-1503, ATCC) in culturing the inner mass cell.

1) The present invention is not obvious from Thomson *et al.*

Thomson et al. disclose the production of a stem cell using a fresh or frozen embryo in the cleavage stage human embryo, while the present invention uses a cryopreserved blastocyst embryo. The Examiner acknowledged this difference in constitution (see page 8, lines 8~9, of the Office Action). Owing to such difference, the present invention is more advantageous both practically and ethically because it can use such cryopreserved zygotes, which are ordinarily discarded after a particular period of time (see page 12 of the present specification).

The present invention also uses anti-human lymphocyte antibodies (hereinafter "AHLS") for removing the trophectoderm from the blastocyst embryo, while Thomson uses conventional anti-human serum antibodies. As explained on pages 8-9 of the present specification, trophectoderm cannot be completely removed from the inner cell mass by the conventional anti-human serum antibodies. In contrast, the AHLS is specially designed for immunosurgery to selectively obtain the inner cell mass (ICM) in the present invention. AHLS can thus be used in the immunosurgery

process to effectively establish human ES cells derived from a frozen-thawed blastocyst stage embryo.

In addition, the conventional mouse embryonic fibroblast (MEF) cells of Thomson et al. need to be newly prepared before use and there are differences among the mice used. The STO cell of the present invention, however, is a permanent cell line and, thus, free of such disadvantages. Thomson *et al.* do not disclose or mention the STO (mouse embryonic fibroblast) cell.

2) The present invention is not obvious from Kaufmann *et al.*

Contrary to the Examiner's assumption, Kaufmann *et al.* simply disclose that cryogenic blastocyst embryo can be used in In Vitro Fertilization (IVF), not in the production of human stem cells as in the present invention.

The technical requirement for In Vitro Fertilization is highly different from that for stem cell production. Kaufmann *et al.*, for example, use intact embryos at the blastocyst stage in implantation. That is, the cryopreserved and then thawed embryo is directly used in IVF. In the present invention, trophectoderm is removed from the blastocyst embryo, thereby isolating the inner mass cell and the resulting inner mass cell is cultured. In this regard, Kaufmann *et al.* are silent on whether blastocyst embryos can be effectively used in stem cell production after removing trophectoderm by immunosurgery.

Thus, the greater viability of cryogenic blastocyst embryos over cleavage stage embryos in IVF does not necessarily indicate that the cryogenic blastocyst embryos can be effectively used in the production of stem cells. Accordingly, the use of blastocyst embryos in the production of stem cells is neither disclosed nor suggested by Kaufmann *et al.*

3) The combination of Thomson and Kaufmann does not lead to the present invention.

As explained above, the idea of using a blastocyst embryo in IVF disclosed by Kaufmann *et al.* cannot be directly applied to the stem cell production disclosed by Thomson *et al.*, because

technical requirement for IVF is different from that for stem cell production. The present invention requires isolation of the inner mass cell from the blastocyst embryo, while Kaufmann *et al.* use intact blastocyst embryos in implantation. Further, Kaufmann *et al.* do not provide any information or suggestion about the isolation of inner mass cell.

Even if the blastocyst embryo in Kaufmann *et al.* can be applied to the stem cell production in Thomson *et al.*, the mere combination of said two references cannot lead to the present invention, because the critical technical features of the present invention are not taught or hinted by said cited references. As mentioned above, the use of anti-human lymphocyte antibodies and STO cells is not disclosed or even suggested in either Thomson *et al.* or Kaufmann *et al.* The present invention therefore is not obvious from said cited references.

In view of the foregoing, Applicant respectfully requests that the 103 rejection be withdrawn.

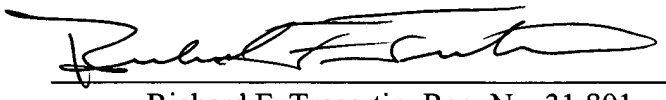
Applicants respectfully submit that the claims are in condition for allowance and an early notification of such is solicited.

Please direct any calls in connection with this application to the undersigned at (415) 781-1989.

Respectfully submitted,

DORSEY & WHITNEY LLP

Date March 4, 2004



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